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## Evaluation of a complex intervention to improve primary care prescribing

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1 **System-wide phase 4 complex intervention to improve primary care prescribing: segmented regression**  
2 **interrupted time-series analysis**

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20 General Practice  
21 interrupted time series analysis  
22 administrative data

23

## 24    **Abstract**

25    **Background:** It is uncertain whether improvements in primary care high-risk prescribing seen in research trials can  
26    be realised in the ‘real-world’ setting.

27    **Aim:** To evaluate the impact of a one-year system-wide phase 4 prescribing safety improvement initiative.

28    **Design and Setting:** Interrupted time-series analysis of targeted high-risk prescribing in all 56 general practices in  
29    NHS Forth Valley, Scotland (in 2013/14: non-steroidal anti-inflammatory drugs (NSAIDs) in older people, the triple  
30    whammy and NSAIDs with oral anticoagulants; in 2014/2015: antipsychotics in older people).

31    **Method:** Primary analysis used segmented regression analysis to estimate impact at the end of the intervention, and  
32    twelve months later. Secondary analysis used difference-in-difference methods to compare Forth Valley changes  
33    with those in NHS Greater Glasgow and Clyde (GGC).

34    **Results:** In primary analysis, downward trends for all three NSAID measures before the intervention significantly  
35    steepened following implementation. At the end of the intervention period, 1,221 fewer patients than expected  
36    were prescribed a high-risk NSAID. In contrast, antipsychotic prescribing in older people increased slowly over time  
37    with no intervention-associated change. In secondary analysis, reductions at the end of the intervention period in all  
38    three NSAID measures were significantly greater in Forth Valley than in GGC, but only significantly greater for two of  
39    these measures twelve months after the intervention finished.

40    **Conclusion:** There were substantial and sustained reductions in high-risk prescribing of NSAIDs, although with some  
41    waning of effect twelve months after the intervention ceased. The same intervention had no effect on antipsychotic  
42    prescribing in older people.

43

44    **Keywords:** quality improvement; phase 4 complex intervention; high-risk prescribing; non-steroidal anti-  
45    inflammatory drugs (NSAIDs); antipsychotic drugs; General Practice, interrupted time series analysis; administrative  
46    data

There is good evidence from phase 3 cluster-randomised trials that a number of interventions reduce high-risk prescribing in primary care, but whether similar improvements can be realised in the 'real-world' setting is less clear.

A system-wide quality improvement intervention combining education, feedback, support to identify patients to review, and small financial incentives resulted in large reductions in high-risk prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) of a similar magnitude to those seen in phase 3 trials.

Phase 3 trials rarely examine what happens after the intervention ends, but in this study there was evidence that the effect on high-risk NSAID prescribing waned somewhat in the year after the intervention ended, highlighting the need for healthcare improvement to monitor impact longer term and consider interventions to sustain benefit.

There was no effect of the same intervention on high-risk prescribing of oral antipsychotics, highlighting that interventions may have differential effectiveness depending on the wider context of prescribing (in this case, NSAID prescribing is 'owned' by general practitioners but antipsychotic prescribing is usually specialist initiated).

## 49 Introduction

50 High-risk prescribing is common in primary care<sup>1,2</sup> although it is not always inappropriate since expected benefit can  
51 outweigh expected harm in individual patients. Drugs commonly implicated in preventable adverse drug events  
52 (ADEs) resulting in hospital admissions include non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin which are  
53 responsible for 30% of ADE-related hospital admissions, due to bleeding, stroke, and renal injury.<sup>3</sup> Similar to primary  
54 care organisations elsewhere, Health Boards in Scotland use a variety of means to try to influence primary care  
55 prescribing, including education and feedback, pharmacist-support, and small financial incentives.<sup>4,5</sup> Historically, the  
56 focus of most of this work has been on controlling prescribing costs,<sup>6</sup> but the growing availability of better  
57 prescribing data opens up new opportunities to target quality and safety such as the NHS Forth Valley intervention  
58 to improve primary care prescribing safety (Box 1).

59 A range of prescribing safety indicators have been developed,<sup>7-9</sup> and interventions to improve subsets of them  
60 evaluated in phase 3 cluster-randomised trials in primary care.<sup>10-13</sup> The PINCER trial evaluated practitioner education,  
61 informatics tools to identify relevant patients, and intensive pharmacist support to review patients and improve  
62 prescribing systems.<sup>11</sup> For the three primary high-risk prescribing outcome indicators (non-selective non-steroidal  
63 anti-inflammatory drugs (NSAIDs) prescribed to those with a history of peptic ulcer without co-prescription of a  
64 proton-pump inhibitor;  $\beta$  blockers prescribed to those with a history of asthma; long-term prescription of  
65 angiotensin converting enzyme (ACE) inhibitor or loop diuretics to those 75 years or older without assessment of  
66 urea and electrolytes in the preceding 15 months) there was a reduction in the odds of each of of 27-49% at 6  
67 months, which diminished to 9-37% by 12 months. The DQIP trial evaluated education, informatics to support  
68 patient identification, and financial incentives for patient review.<sup>12</sup> There was a 41% reduction in the odds of the  
69 composite measure of targeted high-risk prescribing at one year, sustained in the following year. The lower-intensity  
70 EFIPPS intervention had a 14% reduction in the odds of six measures of high-risk NSAID and antipsychotic prescribing  
71 after five rounds of quarterly feedback.<sup>13</sup> However, whether these improvements can be replicated in everyday  
72 practice is uncertain. The UK Medical Research Council recommends phase 4 evaluation to “determine whether  
73 others can reliably replicate your intervention and results in uncontrolled settings over the long term”<sup>10</sup> since  
74 “effects are likely to be smaller and more variable once the intervention becomes implemented more widely, and ...  
75 long-term follow-up may be needed to determine whether short-term changes persist.”<sup>14</sup> The aim of this phase 4  
76 study is to evaluate the impact of a complex, whole system real-world intervention to improve prescribing safety  
77 implemented in all practices in a Scottish Health Board region with a population ~300,000, including whether impact  
78 was sustained post-intervention.

## 79    **Methods**

80    The overall design is segmented regression analysis of interrupted time series data from a Scottish Health Board  
81    implementing the intervention, and a comparator Scottish Health Board that did not. There are ~300,000 registered  
82    patients in the intervention Health Board (NHS Forth Valley) and ~1,200,000 registered patients in the neighbouring  
83    comparator Health Board (NHS Greater Glasgow and Clyde [GGC]).

### 84    *Data Source*

85    Data on prescriptions dispensed by community pharmacies between April 2009 and September 2015 were extracted  
86    from the NHS Scotland Prescribing Information System (PIS). 94.7% of dispensed prescriptions in NHS Forth Valley  
87    and 94.5% in NHS GGC have an associated unique patient identifier, allowing the construction of patient-level  
88    prescribing histories and the identification of co-prescribing in individuals.

### 89    *Interventions and outcomes*

90    In financial year 2013/14, NHS Forth Valley implemented a prescribing improvement intervention targeting three  
91    high-risk NSAID prescribing measures as part of their annual Whole System Working (WSW) primary care  
92    improvement programme (box 1). The WSW intervention included education, feedback, searches and pharmacist  
93    support to identify relevant patients from electronic health records, and financial incentives for practices to report  
94    any changes in the high-risk prescribing rates to the Health Board at year-end. In 2014/2015, a new measure  
95    (antipsychotic use in people aged 75 years and over) replaced the NSAID measures targeted in the previous year. The  
96    prescribing measures used in the intervention and evaluation were ones used in the EFIPPS trial<sup>13</sup> (that neither Forth  
97    Valley nor GGC participated in), and are shown in table 1.

98    Over the same period, NHS Greater Glasgow and Clyde (GGC) chose to focus on other areas of prescribing  
99    improvement, including medication review in older people with polypharmacy at risk of re-admission to hospital.  
100    High risk prescribing of NSAIDs and oral antipsychotics was included in the medication review guidance but there  
101    was no specific targeting of the measures used in Forth Valley.<sup>15</sup> Within each Health Board more than 95% of  
102    practices participated in these activities.

### 103    *Statistical analysis*

104    The primary analysis used segmented regression of interrupted time-series (ITS) data to examine the impact of the  
105    implementation and withdrawal after one year of the WSW intervention in Forth Valley. The intervention period  
106    started at the beginning of quarter 2 (April) of the relevant year, and finished at the end of quarter 1 of the next year  
107    (March) (table 1). For each measure in Forth Valley, the trend before each interruption, step-changes immediately  
108    after intervention period start and end, and changes in trend following the start and end of the intervention period  
109    were estimated. Model estimates were used to calculate the intervention effect (by subtracting the observed value  
110    from the predicted value if prior trends had continued) at the end of the 12 month intervention period, and at 12

months after the intervention period ended.<sup>16 17</sup> The overall intervention effect of the three measures of high-risk NSAID prescribing was estimated using a composite of all three that accounted for some patients having multiple risk factors. Secondary analyses compared changes in NHS Forth Valley with changes in the same prescribing measures in the same period in NHS GGC. For this analysis, a segmented regression model was fitted for the difference between rates in the two Health Boards (Forth Valley minus GGC), allowing estimation of the difference-in-differences of change in Forth Valley relative to change in GGC (appendix A).<sup>18</sup>

For the three NSAID measures there were 16 quarterly time-points before the intervention start, four during the intervention period, and eight after the intervention period. For the antipsychotics in older people measure, there were 20 quarterly time-points before, four during and four after the intervention period. Modelling accounted for autocorrelation by using the Cumby-Huizinga general test and fitting lag terms to models as required. Newey-West standard errors were estimated to account for autocorrelation and possible heteroscedasticity.<sup>19</sup> Statistical analysis was undertaken using Stata v13.1 (Statacorp, College Station, Texas).

## Results

### *NHS Forth Valley NSAIDs 2013-14*

All three NSAID measures had a statistically significant downward trend before the implementation of WSW between April 2013 and March 2014. Following the implementation start at April 2013 there was no immediate change in the rate of prescribing for the triple whammy and NSAIDs in older people measures, but the existing downward trends significantly steepened (table 2; figure 1). For NSAIDs with OAC, there was a statistically significant immediate decrease in prescribing, but no significant change in trend. At the end of the intervention period in April 2014, there was a statistically significant immediate increase in both triple whammy and NSAID prescribing in older people, but not for NSAIDs with OAC. After the end of the intervention period, there were statistically significant changes in trend leading either to a reversion to pre-intervention downward trends (triple whammy) or a diminished intervention effect (NSAIDs in older people and NSAIDs with OAC).

Compared to rates predicted based on pre-intervention trends, the estimated relative effect at the end of the intervention period in April 2014 was a 55.4% (95% CI 43.6 to 67.2) reduction for the triple whammy measure, a 69.9% (95% CI 59.6 to 80.2) reduction for NSAIDs in older people, and a 55.1% (95% CI 27.0 to 83.2) reduction for NSAIDs with OAC. The relative impact 12 months after the intervention period ended in April 2015 was still substantial but somewhat smaller: reductions of 42.7% (95% CI 27.4 to 58.0), 40.1% (95% CI 26.4 to 53.8) and 27.6% (-11.4 to 66.7, not statistically significant) respectively (table 3).

Pre-intervention trends in GGC were not significantly different from Forth Valley for the triple whammy and NSAIDs with OAC measures. For NSAIDs in older people there was a small but statistically significant more rapid decline in the pre-intervention trend in Forth Valley than GGC (figure 1, appendix table A1). For the triple whammy measure, at the end of the intervention period in April 2014 there was a reduction of 34.3% (95% CI 26.4 to 42.3) relative to

GGC which diminished over the 12 months after the intervention finished in April 2015 to a reduction of 25.7% (95% CI 15.2 to 36.3) (table 3). For NSAIDs in older people, at the end of the intervention period in April 2014 there was a reduction of 59.4% (95% CI 52.5 to 66.3) relative to GGC reducing to 28.6% (95% CI 18.8 to 38.3) by April 2015 (table 3). For NSAIDs with OAC at the end of the intervention period there was a reduction of 85.0% (95% CI 45.5 to 100) relative to GGC reducing to 69.0% (95% CI 27.2 to 100) by April 2015 (table 3).

The total reduction in the number of patients prescribed triple whammy, NSAIDs in older people or NSAIDs with OAC, accounting for some patients having multiple risk factors, was 1,221 fewer patients than expected at the end of the intervention period at April 2014. At April 2015, 12 months after the intervention ended, there were 751 fewer patients than expected triggering one or more of the three indicators.

#### *NHS Forth Valley antipsychotics 2014-15*

There was a non-significant increase in prescribing of antipsychotics in older people in Forth Valley before the intervention and no statistically significant changes immediately after the WSW intervention was introduced in April 2014. The upward trend significantly steepened at the time the intervention period ended at April 2015 (although in absolute terms the change is small) (table 2; figure 2). There was no significant estimated impact at the end of the intervention period or 12 months later (table 4).

GGC had a higher baseline rate than Forth Valley that was falling rather than rising. At the end of the intervention period in April 2015 Forth Valley had a 11.3% (95% CI 3.6 to 18.9) reduction relative to GGC but this difference was driven by an increase in GGC (figure 2) so is unrelated to the WSW intervention. There was no statistically significant difference 12 months after the end of the intervention period in April 2016 (appendix table A1 and table 3).

## **Discussion**

### *Summary*

The Whole System Working intervention implemented in all Forth Valley practices in 2013/14 led to large (>55%) reductions in the three targeted measures of high-risk NSAID prescribing at the end of the intervention period. There was evidence of a diminished intervention effect 12 months later, but reductions were still substantial. Relative to GGC these observed reductions remained significant, increasing confidence that the intervention was effective. In contrast, the same WSW intervention in 2014/15 was not associated with any change in antipsychotic prescribing in older people. Although there were significant 'reductions' in Forth Valley relative to GGC we interpret the observed 'reduction' as being due to increased prescribing in GGC rather than due to the intervention in Forth Valley.

### *Strengths and limitations*

Interrupted times series analysis (ITSA) is the most robust method available for evaluating non-randomised interventions. This analysis used population-based routine data to examine a system-wide prescribing safety



intervention using ITSA. Secondary comparison with another Health Board (that did not implement specific improvement activity on the targeted prescribing) was consistent with the observed changes in Forth Valley being attributable to the intervention. Limitations include the risk of under-detection of high-risk prescribing because not all prescriptions have a usable unique patient identifier although we would not expect this to alter the interpretation since there was no change in this over time and no difference between the Health Boards. The assumptions of the difference-in-differences model were violated for the antipsychotics in older people measure since there were different prior trends in the two health boards, and we conclude that the intervention had no effect on targeted antipsychotic prescribing. The post intervention period is also relatively short, particularly for the 2014/15 intervention. Finally, we cannot exclude the possibility that the observed associations are due to some other intervention happening at the same time, and the difference in NSAID and antipsychotic outcomes might also be due to changing pressures and priorities in primary care. However, there was no other intervention in Forth Valley during the period examined, and the comparison with GGC provides some reassurance that the Forth Valley intervention caused the observed changes in prescribing.

#### *Comparison with existing literature*

The impact of this real-world intervention on the high risk prescribing of NSAIDs at one year is similar to that observed in the DQIP trial of a more intensive complex intervention.<sup>12</sup> DQIP reduced triple whammy, NSAIDs in older people, and NSAIDs with OAC by 23%, 56% and 69% respectively at the end of the 12 month intervention, compared to 55%, 70% and 55% in NHS Forth Valley (although the measures used in the two studies are not identical in design). The effect size is also similar in magnitude to those observed in the PINCER trial for a different NSAID measure (NSAIDs prescribed to people with a history of peptic ulcer).<sup>11</sup> Like PINCER (but unlike DQIP), there was evidence of some waning of effect once the intervention ceased, although the impact at 12 months after the end of the intervention remained similar in magnitude to DQIP. Changes in NSAID prescribing were substantially larger than those observed in the simpler EFIPPS feedback intervention and it is notable that like this analysis, there was no evidence that the EFIPPS intervention reduced antipsychotic prescribing in older people.<sup>13</sup>

#### *Implications for research and/or practice*

Whether organisational interventions shown to be effective in phase 3 trials will be effective in real-world system-wide implementation is often uncertain, since trials are usually carried out by volunteers and often have higher intensity of intervention supported by research funding.<sup>10, 14</sup> This study shows that a phase 4 intervention reduced high-risk primary care prescribing of NSAIDs to a similar degree as the two previous large phase 3 trials of similar complex interventions in this field. Consistent with the EFIPPS study,<sup>13</sup> this analysis shows that impact may at least partly depend on the prescribing targeted. In Forth Valley, the same intervention was highly effective at reducing high-risk NSAID prescribing but ineffective at reducing antipsychotic prescribing in older people. Neither this study nor the EFIPPS trial can examine why this should be, but one possible explanation is that NSAID prescribing is largely initiated and managed by GPs,<sup>20</sup> whereas antipsychotic prescribing is commonly initiated by specialists plausibly

209 reducing GP ownership of it even when they are responsible for prescribing antipsychotics longer-term. GPs also  
210 report that they continue antipsychotic prescribing in older people because of a sense of futility and concerns about  
211 harm if prescribing is stopped.<sup>21</sup> There is therefore unlikely to be a single ‘magic bullet’ intervention that will be  
212 effective for all high-risk prescribing.

213 *Conclusion*

214 Overall, the findings suggest that a blends of the intervention components used in trials (education, feedback  
215 financial incentives) tailored to a local context are likely to be effective in system-wide implementation. The partial  
216 waning of effect in the year after the intervention ceased highlights that trials should ideally follow-up patients  
217 beyond the duration of the intervention, and that at least some interventions may need to be repeated to be  
218 sustainable. However, the lack of impact on antipsychotic prescribing in older people in this study and in the EFIPPS  
219 trial <sup>13</sup> indicates the need for more research into how best to reduce this prescribing. Although randomised trials will  
220 be helpful in addressing many of these uncertainties, further rigorous evaluations of phase 4 system-wide  
221 implementations would be of great value. The growth of electronic prescribing makes interventions of this kind  
222 increasingly feasible internationally, and the time is ripe for wider implementation to improve prescribing safety.

223

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225

226   **Funding**

227   There was no specific funding for this study (see the competing interests statement).

228   **Ethics**

229   The analysis is a retrospective evaluation of an NHS improvement project using routine NHS administrative data  
230   provided to Health Boards to support improvement and audit, and did not require ethical review.

231   **Competing interests**

232   All authors have completed the ICMJE uniform disclosure form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available  
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236   previous three years; no other relationships or activities that could appear to have influenced the submitted work.

237

**Context of the intervention**

From April 2010 to March 2017 NHS Forth Valley contracted an enhanced service with GP practices called Whole System Working (WSW). WSW in the financial periods of 2013/14 and 2014/15 included an intervention to improve primary care prescribing safety focused on reducing the use of unsafe drug combinations, alongside other activities to improve patient safety, to improve communication between practices, hospital consultants and out-of-hours services, and increasing engagement with locality improvement activity. In each financial year, for completing all WSW work, practices were paid 80p per registered patient per annum (approximately £4000 for an average sized practice of 5000 patients).

**Specifics of the primary care prescribing safety intervention***Targeted high-risk prescribing in 2013/2014:*

Patients aged  $\geq 65$  years prescribed the 'triple whammy' combination (NSAID +ACE/ARB + diuretic)

Patients aged  $\geq 65$  years prescribed an NSAID without gastroprotection

Current anticoagulant user prescribed an NSAID without gastroprotection

*Targeted high-risk prescribing in 2014/2015:*

Patients aged  $\geq 75$  years prescribed an oral antipsychotic

*Educational workshop*

A brief educational intervention focusing on NSAID risks (quarter 2 2013) and antipsychotic risks in older people (quarter 2 2014) lasting approximately 45 minutes was delivered each year in June during a 2.5 hours long educational session on Patient Safety in Primary Care that the majority of GPs attended. This included comparative data on practice rates for that year's measures, and what was expected of practices.

*Feedback and written educational material*

During each year around the same time as the educational workshop each practice was provided written educational material summarising the educational outreach workshop information accompanied by a single round of feedback showing practice rates of targeted high-risk prescribing compared to the average for the Health Board and practices' ranking within the Health Board. The same written material and feedback were given directly to all participants at the educational workshop.

*Financial incentive*

Within each year practices qualified for the WSW payment only when they provided evidence of completing all WSW elements. The evidence required for the high-risk prescribing component was simply to report to the Health Board the number of patients triggering the measures at baseline and 6 months later, rather than provide evidence change in high-risk prescribing rates.

*Support for identification of patients to review*

In both years, practices identified patients for review using search tools supplied by the NHS Forth Valley to run in their own electronic medical record systems. Health Board employed pharmacists reviewed the output of these searches to produce a clean list of patients for GPs to focus on (for example, by checking that the patient had actually received the targeted drug combinations). GPs were asked to review identified patients' records, and then take whatever action they judged appropriate (e.g. continuing, amending or stopping medication without further review; contacting the patient to discuss; etc.). There was no WSW requirement to report to the Health Board the actual action taken.

240 Table 1: Targeted prescribing and outcome measure definition

Measure short name	Measure definition (number of patients in Forth Valley immediately before the intervention started)	Associated harm	Forth Valley intervention period	Prevalence of high-risk prescribing in Forth Valley immediately before the intervention started Rate per 1000 (95% CI)
Triple whammy	Patients aged ≥ 65 years (n=51,595) who are prescribed a diuretic and an ACE inhibitor or angiotensin receptor blocker and an NSAID (n=596)	Acute kidney injury <sup>22, 23</sup>	April 2013 to March 2014	11.6 (10.7 to 12.6) <sup>b</sup>
NSAIDs in older people	Patients aged ≥ 65 years (n=51,595) who are prescribed an NSAID without gastroprotection (n=1,832)	Gastro-intestinal bleeding <sup>24</sup>	April 2013 to March 2014	35.5 (33.9 to 37.1) <sup>b</sup>
NSAIDs with OAC	Patients prescribed an oral anticoagulant (OAC) (n=3,423) who are prescribed an NSAID without gastroprotection (n=23)	Gastro-intestinal bleeding <sup>24</sup>	April 2013 to March 2014	6.7 (4.5 to 10.0) <sup>c</sup>
Antipsychotics in older people <sup>a</sup>	Patients aged ≥ 75 years (n=22,980) who are prescribed an oral antipsychotic (n=512)	Stroke and death <sup>25</sup>	April 2014 to March 2015	22.3 (20.5 to 24.3) <sup>d</sup>

241 a. As a proxy for older people with dementia  
242 b. Rate per 1,000 population aged 65+  
243 c. Rate per 1,000 prescribed an oral anticoagulant  
244 d. Rate per 1,000 population aged 75+

245 Table 2: Forth Valley segmented regression analysis

Prescribing Measures	Baseline rate Patients prescribed per 1,000 at risk (95% CI)	Trend before the intervention period, change in rate per quarter (95% CI)	Immediate step-change in rate at the start of the intervention period (95% CI)	Change in trend after the start of the intervention period, change in rate per quarter (95% CI)	Immediate step-change in rate at the end of the intervention period (95% CI)	Change in trend after the end of the intervention period, change in rate per quarter (95% CI)	Absolute difference at the end of the intervention period, patients prescribed per 1,000 at risk (95% CI)	Absolute difference 12 months after the end of the intervention period, patients prescribed per 1,000 at risk (95% CI)
<b>2013-14 Outcome Measures from Whole System Working in NHS Forth Valley</b>								
Triple whammy - patients aged 65+ years prescribed an NSAID and an ACE/ARB and a diuretic <sup>a</sup>	13.1 (12.4 to 13.8)	-0.2 (-0.2 to -0.1)	-0.5 (-1.3 to 0.3)	-1.2 (-1.4 to -1.1)	1.5 (1.1 to 1.9)	1.3 (1.2 to 1.3)	-5.5 (-6.7 to -4.3)	-4.0 (-5.4 to -2.6)
NSAIDs in older people - patients aged 65+ years prescribed an NSAID without gastroprotection <sup>a</sup>	44.1 (42.9 to 45.4)	-0.7 (-0.9 to -0.6)	-1.6 (-3.8 to 0.6)	-4.6 (-4.95 to -4.3)	7.4 (6.2 to 8.5)	5.2 (4.9 to 5.6)	-20.1 (-23.0 to -17.1)	-10.3 (-13.9 to -6.8)
NSAIDs with OAC - patients prescribed an oral anticoagulant and a NSAID without gastroprotection <sup>b</sup>	9.1 (8.1 to 10.1)	-0.2 (-0.3 to -0.04)	-2.0 (-3.6 to -0.3)	-0.3 (-0.8 to 0.2)	0.6 (-0.8 to 2.0)	0.6 (0.1 to 1.1)	-3.3 (-4.9 to -1.6)	-1.5 (-3.5 to 0.6)
<b>2014-15 Outcome Measure from Whole System Working in NHS Forth Valley</b>								
Antipsychotics in older people - patients aged 75+ prescribed an oral antipsychotic <sup>c</sup>	19.6 (18.7 to 20.5)	0.1 (-0.01 to 0.1)	-0.1 (-1.1 to 0.8)	0.1 (-0.1 to 0.3)	-0.6 (-1.4 to 0.2)	0.3 (0.1 to 0.6)	0.2 (-1.2 to 1.5)	1.2 (-0.5 to 2.9)

246 a. Rate per 1,000 of the population aged 65+  
247 b. Rate per 1,000 prescribed an oral anticoagulant  
248 c. Rate per 1,000 of the population aged 75+  
249

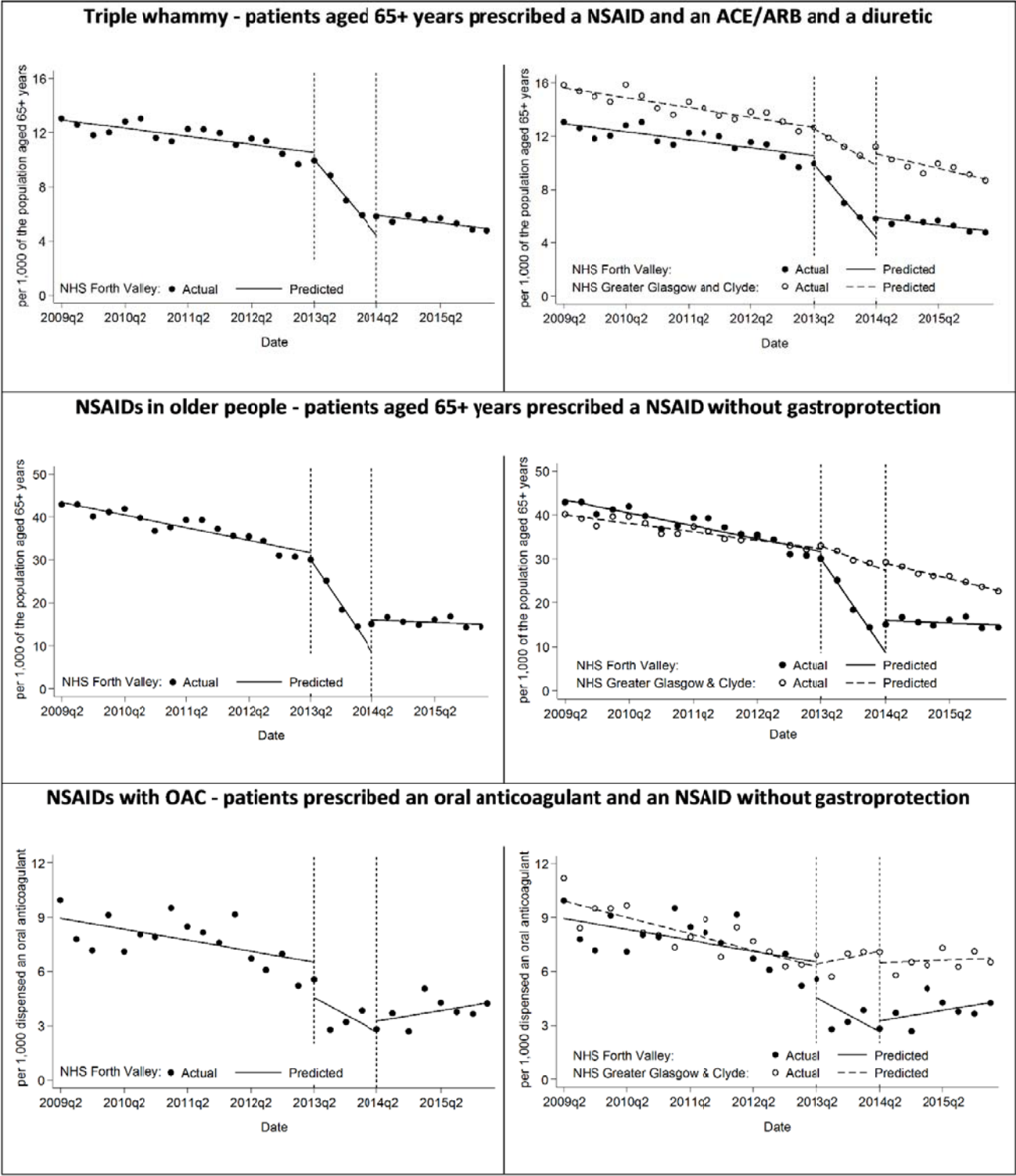
Table 3: Relative effect size in changed rates of high risk prescribing in NHS Forth Valley and for the difference between NHS Forth Valley and NHS GGC

Prescribing Measures	NHS Forth Valley		Difference between NHS Forth Valley and NHS GGC	
	Relative difference (%) from predicted at the end of the intervention period (95% CI)	Relative difference (%) from predicted 12 months after the end of the intervention period (95% CI)	Relative difference (%) compared to GGC at the end of the intervention period (95% CI)	Relative difference (%) compared to GGC 12 months after the end of the intervention period (95% CI)
<b>2013-14 Outcome Measures from Whole System Working in NHS Forth Valley</b>				
Triple whammy -patients aged 65+ years prescribed an NSAID and an ACE/ARB and a diuretic <sup>a</sup>	-55.4 (-67.2 to -43.6)	-42.7 (-58.0 to -27.4)	-34.3 (-42.3 to -26.4)	-25.7 (-36.3 to -15.2)
NSAIDs in older people - patients aged 65+ years prescribed an NSAID without gastroprotection <sup>a</sup>	-69.9 (-80.2 to -59.6)	-40.1 (-53.8 to -26.4)	-59.4 (-66.3 to -52.5)	-28.6 (-38.3 to -18.8)
NSAIDs with OAC - patients prescribed an oral anticoagulant and a NSAID without gastroprotection <sup>b</sup>	-55.1 (-83.2 to -27.0)	-27.6 (-66.7 to 11.4)	-85.0 (-100 to -45.5)	-69.0 (-100 to -27.2)
<b>2014-15 Outcome Measure from Whole System Working in NHS Forth Valley</b>				
Antipsychotics in older people - patients aged 75+ prescribed an oral antipsychotic <sup>c</sup>	0.8 (-5.7 to 7.2)	5.6 (-2.3 to 13.5)	-11.3 (-18.9 to -3.6)	-2.0 (-10.4 to 6.5)

a. Rate per 1,000 of the population aged 65+

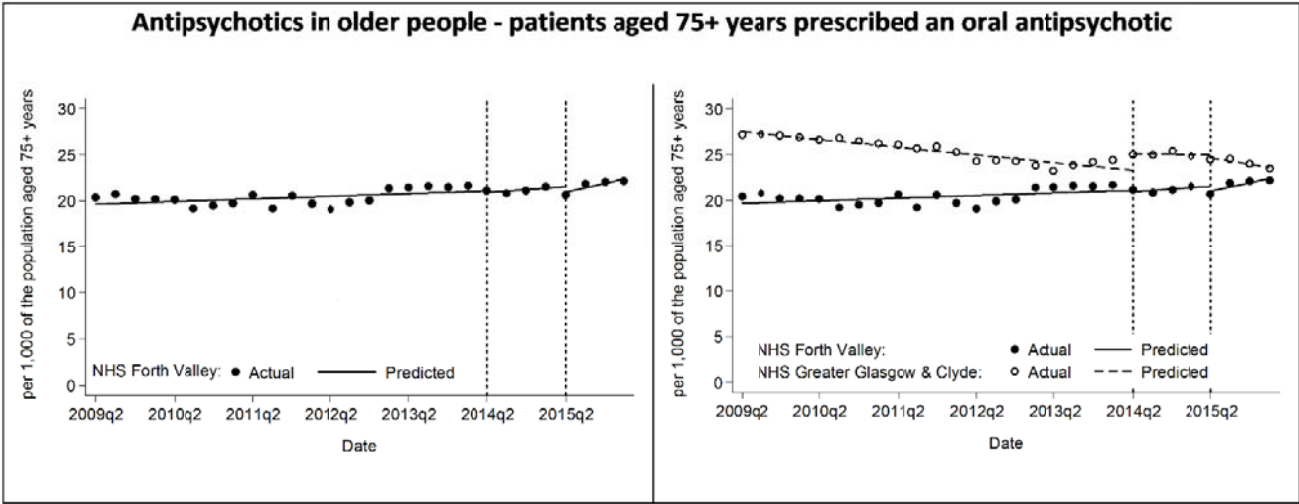
b. Rate per 1,000 prescribed an oral anticoagulant

c. Rate per 1,000 of the population aged 75+



2013-14 Outcome Measures from Whole System Working in NHS Forth Valley  
Figure 1





2014-15 Outcome Measure from Whole System Working in NHS Forth Valley  
Figure 2

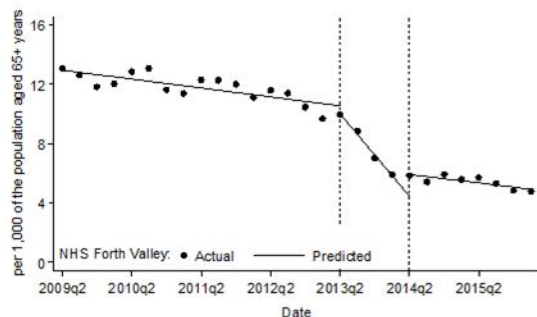
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### Triple whammy - patients aged 65+ years prescribed a NSAID and an ACE/ARB and a diuretic

#### Relative difference from predicted (95% CI):

Significant 55.4% reduction at the end of the intervention period

Significant 42.7% reduction 12 months after the end of the intervention period

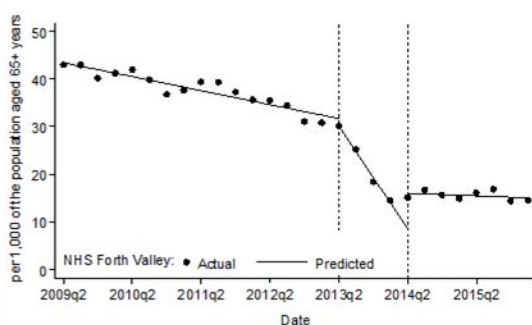


### NSAIDs in older people - patients aged 65+ years prescribed a NSAID without gastroprotection

#### Relative difference from predicted (95% CI):

Significant 69.9% reduction at the end of the intervention period

Significant 40.1% reduction 12 months after the end of the intervention period

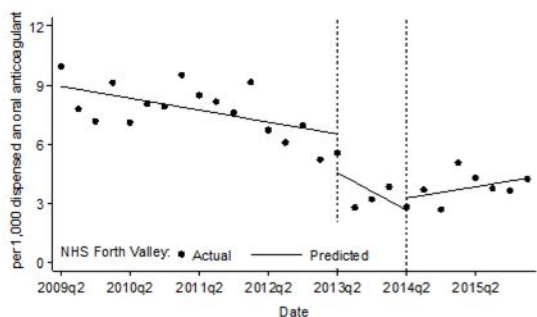


### NSAIDs with OAC - patients prescribed an oral anticoagulant and an NSAID without gastroprotection

#### Relative difference from predicted (95% CI):

Significant 55.1% reduction at the end of the intervention period

Non-significant 27.6% reduction 12 months after the end of the intervention period

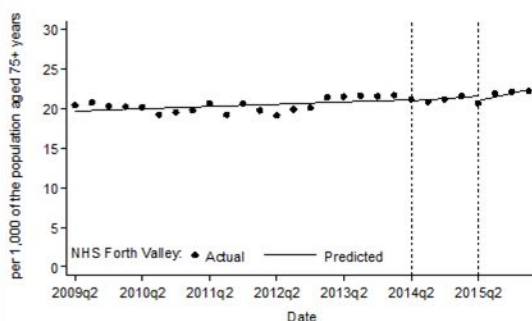


### Antipsychotics in older people - patients aged 75+ years prescribed an oral antipsychotic

#### Relative difference from predicted (95% CI):

Non-significant 0.8% increase at the end of the intervention period

Non-significant 5.6% increase at 12 months after the end of the intervention period



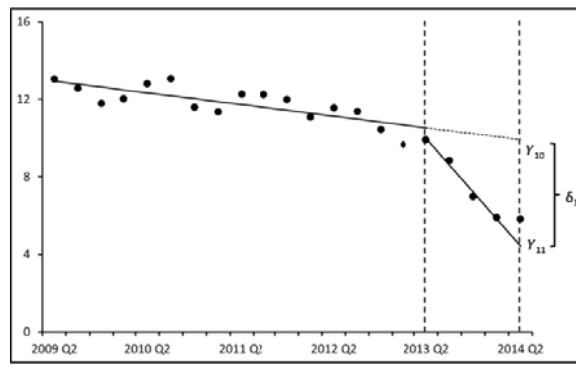
#### Notes

- vertical dotted lines indicate the start and finish times for the one-year system-wide phase 4 prescribing safety improvement initiative

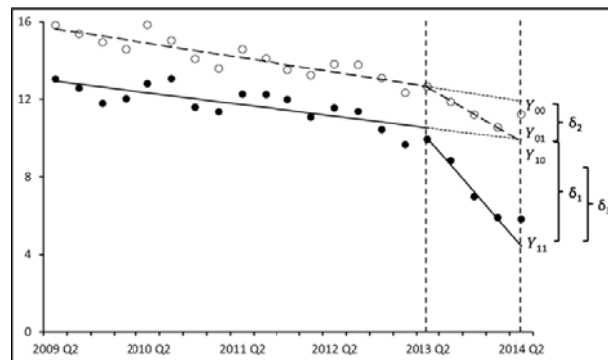
## **APPENDIX A: Primary and secondary analysis estimates of absolute and relative change, and detailed results of the difference in differences analysis**

Figure A1 illustrates the primary analysis estimating the intervention effect size ( $\delta_1$ ) at the end of the intervention period. This is the difference between the rate predicted at the end of the intervention period if the pre-intervention trends continued unchanged ( $Y_{10}$ ), and the rate predicted at the end of intervention period using the intervention period observed values ( $Y_{11}$ ).

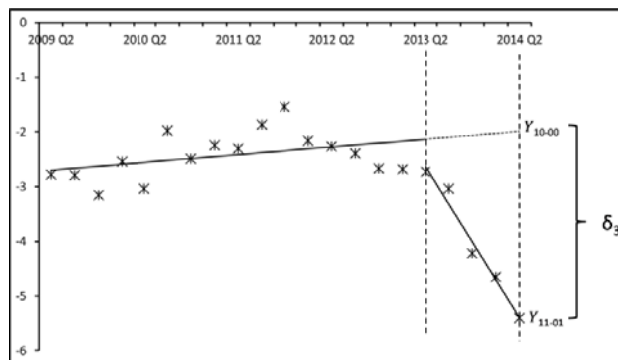
Figure A2 shows the trends in both Health Boards for the same measure. The difference in differences estimate ( $\delta_3$ ) is the difference between the change in Forth Valley ( $\delta_1$ ) and the change in GGC ( $\delta_2$ ). In practice, it is more straightforward to fit a model to the single line that is the difference between Forth Valley and GGC at every time point (figure A3). The difference in differences analysis is then the same as the primary analysis in figure A1, with the impact at the end of the intervention period being the difference in differences estimate ( $\delta_3$ ) described above.



Observed and predicted values in Forth Valley  
Figure A1



Observed and predicted values in Forth Valley and Greater Glasgow and Clyde  
Figure A2



Observed and predicted values of the difference between Forth Valley and GGC at every time point  
Figure A3

Table A1: Differences in high risk prescribing between NHS Forth Valley and NHS GGC<sup>1</sup>

Prescribing Measures	Baseline rate Patients prescribed per 1,000 at risk (95% CI)	Trend before the intervention period, change in rate per quarter (95% CI)	Immediate step-change in rate at the start of the intervention period (95% CI)	Change in trend after the start of the intervention period, change in rate per quarter (95% CI)	Immediate step-change in rate at the end of the intervention period (95% CI)	Change in trend after the end of the intervention period, change in rate per quarter (95% CI)	Absolute difference at the end of the intervention period, patients prescribed per 1,000 at risk (95% CI)	Absolute difference 12 months after the end of the intervention period, patients prescribed per 1,000 at risk (95% CI)
<b>2013-14 Outcome Measures from Whole System Working in NHS Forth Valley</b>								
Triple whammy - patients aged 65+ years prescribed an NSAID and an ACE/ARB and a diuretic <sup>a</sup>	-2.7 (-3.2 to -2.3)	0.04 (-0.02 to 0.1)	-0.5 (-1.1 to 0.1)	-0.7 (-0.8 to -0.7)	0.6 (0.1 to 1.1)	0.8 (0.7 to 0.95)	-3.4 (-4.2 to -2.6)	-2.4 (-3.4 to -1.4)
NSAIDs in older people - patients aged 65+ years prescribed an NSAID without gastroprotection <sup>a</sup>	3.6 (2.6 to 4.6)	-0.3 (-0.4 to -0.1)	-2.2 (-3.8 to -0.7)	-3.7 (-3.8 to -3.6)	5.7 (5.0 to 6.4)	4.7 (4.5 to 4.9)	-17.1 (-19.1 to -15.1)	-7.4 (-9.9 to -4.9)
NSAIDs with OAC - patients prescribed an oral anticoagulant and a NSAID without gastroprotection <sup>b</sup>	-1.0 (-2.3 to 0.2)	0.1 (-0.04 to 0.2)	-2.1 (-3.6 to -0.6)	-0.7 (-1.3 to -0.2)	1.2 (-1.0 to 3.5)	0.8 (0.1 to 1.4)	-5.0 (-7.4 to -2.7)	-3.7 (-5.9 to -1.4)
<b>2014-15 Outcome Measure from Whole System Working in NHS Forth Valley</b>								
Antipsychotics in older people - patients aged 75+ prescribed an oral antipsychotic <sup>c</sup>	-8.1 (-9.2 to -7.0)	0.3 (0.2 to 0.4)	-1.9 (-3.1 to -0.7)	-0.1 (-0.4 to 0.2)	-0.2 (-1.2 to 0.7)	0.7 (0.4 to 0.9)	-2.4 (-4.0 to -0.8)	-0.4 (-2.3 to 1.4)

a. Rate per 1,000 of the population aged 65+

b. Rate per 1,000 prescribed an oral anticoagulant

c. Rate per 1,000 of the population aged 75+

<sup>1</sup> For each time point value the difference between Forth Valley and GGC is calculated. For triple whammy the rate of prescribing at baseline in Forth Valley is 2.7 lower than GGC, there is no difference in the trend prior to the intervention period (both are downward trends), and there is no difference in the change of rate at the start of the intervention period. The trend following the start of the intervention period declines more rapidly in Forth Valley than in GGC (-0.7 per quarter) and at the end of the intervention period the rate in FV increases compared to GGC (0.6). Following the end of the intervention period the prescribing trend increases more rapidly in Forth Valley than in GGC (0.8 per quarter). At the end of the intervention period and 12 months later the rate of prescribing is lower in Forth Valley compared to GGC (-3.4) and (-2.4) respectively.